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ORIGINAL ARTICLE

Hypertensive Disorders in Pregnancy Requiring Emergency (108) Transportation in the State of Gujarat (India): An Epidemiological Study

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ABSTRACT

Objectives: To determine population-based rates and outcomes of hypertensive disorders in pregnancy requiring emergency medical transportation in the state of Gujarat (India).

Design: Cross-sectional study using linked population databases.

Setting and participants: All women and their babies who were catered to by emergency (108) ambulances and were discharged from hospital following birth in the state of Gujarat, (India), between 1st June 2008 and 31st December 2008.

Main outcome measures: Rates of hypertensive disorders in pregnancy, maternal and infant morbidity and mortality and level of hospital care for birth admission.

Results: 250 173 women and their 255 931 infants were included in the study. Overall, 24 517 women (9.8%) had a hypertensive disorder in pregnancy, including 1411 (0.6%) with chronic hypertension, 10 379 (4.2%) with pre-eclampsia, 731 (0.3%) with chronic hypertension with superimposed pre-eclampsia and 10 864 (4.3%) with gestational hypertension. Women with and infants exposed to hypertension were more likely to suffer death or major morbidity than those without hypertension. Infants of mothers with hypertension were more likely to be born preterm and were small for their gestational age. Just over half the women with major morbidity or mortality delivered in hospitals with a high level of medical care. In contrast, most infants with major morbidity or mortality were delivered in hospitals with neonatal intensive care units.

Conclusions: Hypertension is a common complication of pregnancy and adverse outcomes are increased among hypertensive women and their babies. Clinicians appear to be better at identifying and seeking an appropriate level of care for pregnancies where the infant is at risk of a poor outcome than when the mother is at risk. More specific antenatal indicators of poor maternal outcome would help guide the referral of hypertensive women to higher levels of care.

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Pregnancies which are complicated by hypertension are associated with an increased risk of adverse foetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction, perinatal death, acute renal or hepatic failure, antepartum haemorrhage, postpartum haemorrhage and maternal death [1],[2],[3].The term “hypertensive disorders in pregnancy” encompasses two different,

but related, conditions[1],[2],[3]. Chronic hypertension predates the pregnancy or has onset before 20 weeks of gestation. Hypertension arising *de novo* in pregnancy from 20 weeks of gestation ranges from hypertension alone (gestational hypertension) through proteinuria and multiorgan dysfunction (pre-eclampsia), to seizures (eclampsia). Some women with chronic hypertension develop superimposed pre-eclampsia.

In 1989, Collins and Wallenburg [3] commented that “there are surprisingly few population- based studies of the frequency with which hypertensive disorders occur in pregnancy” and little has changed since then [4],[5],[6]. Furthermore, there are no population-based studies on the maternal morbidities associated with hypertension in pregnancy in India. The aim of our study was to determine the current rates and outcomes of hypertensive disorders in pregnancy in a statewide population.

Methods

Study population

The study population included all women and their babies who were catered to by emergency (108) ambulances and were discharged from hospital following birth in the state of Gujarat (India), between 1st June 2008 and 31st December 2008. Only 1% of the women had homebirths.

Datasets

The data were obtained from the variance database of the Emergency Management and Research Institute (EMRI) and from the datasets of the Department of Health and Family Welfare, Government of Gujarat (GOG). The dataset of the Department of Health and Family Welfare, Government of Gujarat, is a population-based surveillance system covering all births of > 20 weeks of gestation or > 400 g birth weight in the state of Gujarat. It includes information on maternal characteristics, pregnancy, labour, delivery and infant outcomes. The dataset of

the Department of Health and Family Welfare, Government of Gujarat, is a census of all Gujarat inpatient hospital separations; the data are coded from the medical records according to the 10th revision of the *International statistical classification of diseases and related health problems* (ICD-10) [8],[9].The Emergency Management and Research Institute (EMRI) performed the record linkage of the two datasets and produced de-identified, linked birth and hospital records. The linkage proportions for the two datasets were > 97%.

Hypertension is reported in both the EMRI and the GOG databases. There are six major ICD-10 codes for hypertension and the GOG includes at least 21 ICD-10-coded diagnoses for each hospital admission. Validation of hypertension reporting in both datasets against medical records found the specificity to be very high (> 99%), indicating few false positive diagnoses.[10,11] However, both datasets suffer from under-reporting (sensitivities 50%–86%) and misclassification of gestational hypertension and pre-eclampsia [10],[11]. Identifying cases from both birth and hospital separation data resulted in a higher sensitivity than that obtained from identifying cases from either birth or hospital separation data alone [12],[13]. Therefore, identification of hypertension during pregnancy in either dataset was considered a “case”.

Classification of Hypertension

Hypertension was classified in mutually exclusive categories:

- chronic hypertension,
- pre eclampsia/eclampsia,
- chronic hypertension with superimposed pre-eclampsia,
- gestational hypertension,
- hypertension (unspecified).

When there was an inconsistency in the type of hypertension reported in the two datasets, the selection of the hypertension type was based on maximizing the likelihood of

accurate diagnosis. Therefore, the selection was based on positive predictive values (PPV: the probability that a reported case is truly a case) from the validation studies and the conformity of the datasets with accepted diagnostic criteria was in the following order of preference: GOG pre-eclampsia, GOG gestational hypertension, EMRI pre-eclampsia, GOG chronic hypertension and EMRI chronic hypertension [10],[11]. For example, records coded as gestational hypertension in the GOG and as pre-eclampsia in the EMRI were classified as gestational hypertension. Women with hypertension were compared with women without hypertension for pregnancy characteristics and outcomes. Outcomes for infants exposed to maternal hypertension were compared with infants who were not exposed to hypertension. “Severe postpartum haemorrhage” (PPH) included PPH in conjunction with a transfusion, hysterectomy, disseminated intravascular coagulopathy, acute renal failure, or admission to intensive care. “Major maternal morbidity or mortality” included antepartum haemorrhage, severe PPH, eclampsia, acute renal or hepatic failure, intracranial haemorrhage, admission to intensive care or maternal death in the hospital. We considered that large district hospitals and perinatal centers (with tertiary obstetric and neonatal care) could provide an appropriate level of medical care for these women. “Major neonatal morbidity or mortality” included gestation at < 33 weeks, Apgar score < 4 at 5 minutes, transfer to higher care, admission to neonatal intensive care, or neonatal death. These infants would require care at a perinatal centre.

Statistical Analysis

Rates were calculated per 100 women (or babies) and women with hypertension were compared with women without hypertension by using the χ^2 test with a significance level set at $P < 0.01$. Maternal-age-adjusted foetal death rates were calculated by direct standardisation using the study population as the standard. Analyses were conducted using the SAS statistical software.

Ethics Approval

The study was approved by the Emergency Management and Research Institute Review Committee.

Results Women

Linked GOG-EMRI records were available for 250,173 women over the study period. The rate of hypertensive disorders was 7.2% in the EMRI, 8.6% in the GOG and 9.8% based on a report in either dataset. Among the 250,173 records, 815 had inconsistent reporting of chronic and de-novo hypertension and 5558 had hypertension recorded in one dataset and not in the other. Pregnancy characteristics and outcomes for the women are shown in [Table/Fig 1]. Of the 24, 517 (9.8%) women had hypertension, 1411 (0.6%) had chronic hypertension, 10 379 (4.2%) had pre-eclampsia, 731 (0.3%) had chronic hypertension with superimposed pre-eclampsia, 10 864 (4.3%) had gestational hypertension and 1132 (0.5%) had hypertension of an unspecified type. One hundred and sixty one women (0.064%) were reported to have eclampsia. Women with chronic hypertension (with or without pre-eclampsia) were older, on an average, than women without hypertension, while those with pre-eclampsia or gestational hypertension had a similar age distribution as women without hypertension. The proportion of nulliparous women also varied according to the type of hypertension. When compared with women who did not have hypertension, women with hypertensive disorders were more likely to have an elective delivery (induction of labour or caesarean section without labour). Women with pre-eclampsia (with or without chronic hypertension) or gestational hypertension were more likely to deliver in a large district hospital or tertiary hospital than women with no hypertension or chronic hypertension alone. Ten women died over the study period. Six deaths (27.3/100 000) occurred among women with pre-eclampsia

(with or without chronic hypertension) or gestational hypertension and four deaths (1.8/100 000) occurred in women without hypertension ($P < 0.0001$), although the cause of death was unknown. Most maternal morbidities occurred infrequently among all groups of women. Women with pre-eclampsia or gestational hypertension were more likely to suffer major morbidities than women without hypertension. Of the women who died or suffered major morbidity, only those with pre-eclampsia (with or without chronic hypertension) had higher rates of delivery at large district hospitals or perinatal centers.

(Table/Fig 1) Distribution of pregnancy characteristics and outcomes, by type of hypertensive disorder (figures represent percentages of women)

Pregnancy characteristics and outcomes	Chronic hypertension (n=1411)	Pre-eclampsia (n=10379)	Chronic hypertension with superimposed pre-eclampsia (n=731)	Gestational hypertension (n=10864)	No hypertension (n=225656)
Maternal age					
< 20 years	2.0 [†]	4.6	1.6 [†]	4.9 [*]	4.4
20-34 years	65.4 [†]	77.0	68.5 [†]	76.6 [*]	77.6
≥ 35 years	32.6 [†]	18.5	29.8 [†]	18.5	18.0
Nulliparous	35.3 [†]	61.2 [†]	45.1 [†]	55.2 [†]	40.1
Delivery hospital					
Small rural/district	30.8	28.4 [†]	23.0 [†]	29.6 [†]	33.8
Large district/tertiary	46.3	53.5 [†]	65.9 [†]	47.9 [†]	44.0
Private	23.0	18.2 [†]	11.1 [†]	22.5	22.2
Induction of labour	37.9 [†]	52.3 [†]	48.7 [†]	55.8 [†]	21.5
Mode of delivery					
Spontaneous vaginal birth	54.7 [†]	46.7 [†]	44.2 [†]	56.5 [†]	67.7
Instrumental	10.0	13.5 [†]	8.6	14.3 [†]	10.3
Caesarean section during labour	13.3 [†]	17.8 [†]	16.7 [†]	16.1 [†]	9.8
Caesarean section, no labour	22.0 [†]	22.0 [†]	30.5 [†]	13.1 [*]	12.2
Antepartum haemorrhage	0.9	1.5 [†]	1.4	0.9	0.8
Postpartum haemorrhage (PPH)					
Any PPH	6.3	8.1 [†]	6.7	7.9 [†]	5.9
Severe PPH	0.8	1.6 [†]	1.0	0.9 [†]	0.7
Acute renal or hepatic failure	0.1	0.5 [†]	0.4 [*]	0.2 [†]	0.1
Intracranial haemorrhage	0.0	0.1 [†]	0.0	0.0	0.0
Intensive care admission	0.3	2.0 [†]	2.2 [†]	0.3 [†]	0.1
Major maternal morbidity or mortality	1.8	6.4 [†]	4.8 [†]	2.1 [†]	1.6
Delivery hospital for women with major morbidity or mortality	(n=26)	(n=659)	(n=35)	(n=227)	(n=3639)
Small rural/district	30.8	24.3 [†]	8.6 [†]	26.4	30.8
Large district/tertiary	57.7	62.1 [†]	88.6 [†]	53.7	54.6
Private	11.5	13.7	2.9	19.8	14.7

* $P < 0.01$, † $P < 0.001$, ‡ $P < 0.0001$ for comparison of women with hypertension and women without hypertension.

Infants

Outcomes for the babies of women who were included in the study are shown in [Table/Fig 2]. There were 255 931 infants with matched records. Babies of women with chronic hypertension had the highest

foetal death rate (>20weeks) and babies of women with gestational hypertension had the lowest. Maternal- age-adjusted foetal death rates for chronic hypertension and pre-eclampsia were 1.18% and 0.6%, respectively.

All other infant outcomes were examined among the 254 416 live-born infants. The neonates of women with hypertensive disorders were more likely to suffer adverse outcomes than those of women without hypertension, especially neonates whose mothers had chronic hypertension with superimposed pre-eclampsia. The majority of neonates who subsequently died or experienced major neonatal morbidity were born in perinatal centers with tertiary neonatal intensive care units: 66% in the case of neonates of mothers who did not have hypertension, 77% in association with chronic hypertension ($P = 0.03$), 81% in association with pre-eclampsia ($P = 0.0001$), 86% in association with chronic hypertension with superimposed pre-eclampsia ($P = 0.0001$) and 62% in association with gestational hypertension ($P = 0.12$). Among the infants of hypertensive women, 42% of the morbidity was observed in neonates born at less than 33 weeks of gestation, of whom 91% were born in perinatal centers.

(Table/Fig 2) Infant outcomes, by mothers' hypertensive disorder status (figures represent percentages of infants)

Infant outcomes	Chronic hypertension (n=1441)	Pre-eclampsia (n=10952)	Chronic hypertension and pre-eclampsia (n=760)	Gestational hypertension (n=11235)	No hypertension (n=230370)
Fetal death	1.32 [†]	0.74	0.39	0.38 [†]	0.59
Preterm birth [§]					
20-32 weeks	2.6 [†]	4.4 [†]	7.0 [†]	0.7 [†]	1.3
33-36 weeks	6.7 [†]	15.2 [†]	15.6 [†]	6.9 [†]	4.7
1 minute Apgar score [¶]					
< 4	4.5 [†]	4.1 [†]	5.0 [†]	3.0 [†]	2.1
4-6	10.6	14.1 [†]	13.7 [†]	12.1 [†]	9.1
5 minute Apgar score [¶]					
< 4	0.4	0.4	0.3	0.3	0.3
4-6	2.0 [*]	2.2 [†]	2.5 [†]	1.8 [†]	1.2
Small for gestational age ^{¶¶}	9.4	14.8 [†]	15.1 [†]	11.7 [†]	9.4
Admission to neonatal intensive care unit ^{††}	4.5 [†]	7.2 [†]	11.5 [†]	2.2	2.3
Death in hospital ^{‡‡}	0.6	0.4	0.7	0.1 [†]	0.3
Major neonatal morbidity or mortality ^{‡‡‡}	6.1 [†]	9.2 [†]	14.1 [†]	3.1	3.3

* $P < 0.01$, † $P < 0.001$, ‡ $P < 0.0001$ for comparison of infants exposed to maternal hypertension with those not exposed; § Rates are among live births; ¶ Small for gestational age is defined as <10th birthweight percentile for gestational age among singletons and twins 22-44 weeks.^{14,15}

Discussion

Our study reports the current population-based rates of hypertensive disorders in pregnancy and the associated rates of maternal and perinatal morbidity and mortality among these pregnancies. The strength of our study lies in the large, validated population datasets, with linkage to improve case ascertainment[12],[13].The use of positive predictive values (from validation studies of the datasets)for the classification of discrepant cases allowed us to select the hypertension reporting that was most likely to be accurate. Such adjustments minimise, but cannot exclude the diagnostic inaccuracies inherent in population datasets.

Conditions which are present, but which do not affect a current admission are not required to be reported in hospital separation data and this probably contributes to the under-reporting of chronic hypertension [9]. In contrast, pre-eclampsia may be over-diagnosed because of the reliance on dipstick testing for proteinuria.[16] As the linked data pertain to birth admission only, maternal and neonatal morbidity and mortality may be under-reported, while antepartum and postpartum haemorrhage are known to be under-reported (reporting sensitivities of 50% and 59%, respectively) [11].

Population rates of major maternal morbidities which are associated with hypertension have not been previously reported. Women with de-novo hypertension in pregnancy were at an increased risk of a major morbidity or mortality, from 30% increased risk for women with gestational hypertension to 400% for women with pre-eclampsia. Furthermore, 60% of maternal deaths during birth admission occurred among 9% of the study population with de-novo hypertension. The frequency of poor maternal and infant outcomes associated with pre eclampsia may explain the high rate of elective delivery in women with this condition. The small-for-gestational-age rate associated with gestational hypertension was lower than that associated with pre-eclampsia, thus suggesting that in-utero

growth is more affected when there is proteinuric hypertension. Combining pre-eclampsia and gestational hypertension in a single de-novo hypertension category would have masked the variation in outcomes for these subpopulations of women.

While mothers with chronic hypertension did not have increased rates of morbidity and mortality, their infants had increased rates of foetal death, admission to neonatal intensive care, and major neonatal morbidity and mortality. The higher foetal death rate and lower preterm birth rate for women with chronic hypertension compared to those with pre-eclampsia may indicate that early elective delivery averts foetal deaths in pre-eclampsia. The presence of chronic hypertension may warrant increased surveillance of foetal health. Furthermore, chronic hypertension with superimposed preeclampsia can produce an acute medical emergency. Clinicians need to be aware that proteinuria associated with chronic hypertension identifies a pregnancy at increased risk. In such cases, closer maternal and foetal surveillance is indicated, together with referral to a higher level of care, if necessary [17].

Pregnancies complicated by pre-eclampsia arising *de novo* or superimposed on chronic hypertension were associated with higher rates of maternal and perinatal morbidity and mortality. Pre-eclampsia presents a potential danger to the mother and infant, and, where time allows, a high level of maternal and neonatal medical care should be sought [1],[18].The high levels of care achieved for women with chronic hypertension and superimposed pre-eclampsia suggest that there is room for improvement in the care of women in other subgroups. However, to recommend that all hypertensive women be managed in large district or tertiary hospitals would mean transferring the care of over 4000 women each year (or one case of maternal morbidity per 32 women transferred). As the personal

and health system costs of such a recommendation would be great, more specific antenatal indicators of poor outcome are required.

Conclusion

In conclusion, our study shows that one in 10 women giving birth in Gujarat suffers from a hypertensive disorder in pregnancy. There is room for improvement in ensuring that women at risk of a poor outcome deliver in hospitals where the most appropriate level of care can be provided.

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